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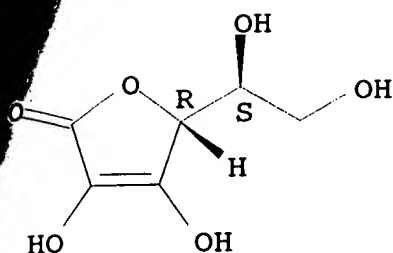
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IC ICM A61K031-725

ICS C08B037-10

NCL 514056000

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 1

IT 50-81-7, Ascorbic acid, reactions

67-68-5, Dms0, reactions 546-67-8, Lead tetraacetate 7790-28-5,

Sodium periodate

(oxidizing agent; heparin fractions for inhibiting thrombogenesis)

L55 ANSWER 6 OF 22 HCA COPYRIGHT 1998 ACS

124:259419 Usefulness of antioxidant vitamins in suspected acute myocardial infarction (the Indian experiment of infarct survival-3). Singh, Ram B.; Niaz, Mohammad A.; Rastogi, Shanti S.; Rastogi, Sharad (Centre Nutrition and Heart Research Laboratory, Medical Hospital and Research Centre, Moradabad, 244001, India). Am. J. Cardiol., 77(4), 232-6 (English) 1996. CODEN: AJCDAG. ISSN: 0002-9149.

AB In a randomized, double-blind, placebo-controlled trial, the effects of combined treatment with the antioxidant vitamins A (50,000 IU/day), vitamin C (1,000 mg/day), vitamin E (400 mg/day), and .beta.-carotene (25 mg/day) were compared for 28 days in 63 (intervention group) and 62 (placebo group) patients with suspected acute myocardial infarction. After treatment with antioxidants, the mean infarct size (creatine kinase and creatine kinase-MB gram equiv.) was significantly less in the antioxidant group than in the placebo group. Serum glutamic-oxaloacetic transaminase decreased by 45.6 IU/dL in the antioxidant group vs. 25.8 IU/dL in the placebo group (p <0.02). Cardiac enzyme lactate dehydrogenase increased slightly (88.6 IU/dL) in the antioxidant group compared with that in the placebo group (166.5 IU/dL) (p <0.01). QRS score in the ECG was significantly less in the antioxidant than in the placebo group. The following levels increased in the antioxidant group vs. the placebo group, resp.: plasma levels of vitamin E increased by 8.8 and 2.2 .mu.mol/L (p <0.01), vitamin C increased by 12.6 and 4.2 .mu.mol/L (p <0.01), .beta.-carotene increased by 0.28 and 0.06 .mu.mol/L (p <0.01), and vitamin A increased by 0.36 and 0.12 .mu.mol/L (p <0.01). Serum lipid peroxides decreased by 1.22

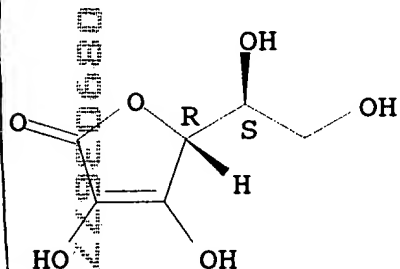
pmol/mL in antioxidant vs. 0.22 pmol/mL in the placebo group ($p < 0.01$). **Angina pectoris**, total arrhythmias, and poor left ventricular function occurred less often in the antioxidant group. Cardiac end points were significantly less in the antioxidant group (20.6% vs 30.6%, resp.). These results suggest that combined treatment with antioxidant **vitamins A, E, C, and .beta.-carotene** in patients with recent acute myocardial infarction may be protective against cardiac necrosis and oxidative stress, and could be beneficial in preventing complications and cardiac event rate in such patients.

IT 50-81-7, **Vitamin c**, biological studies
(usefulness of antioxidant vitamins in suspected acute myocardial infarction)

RN 50-81-7 HCA

CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 18-2 (Animal Nutrition)

IT Heart, disease

(**angina pectoris**, usefulness of antioxidant vitamins in suspected acute myocardial infarction)

IT 50-81-7, **Vitamin c**, biological studies

1406-18-4, **Vitamin e** 7235-40-7, **.beta.-Carotene** 9001-60-9,

Lactate dehydrogenase 11103-57-4, **Vitamin a**

(usefulness of antioxidant vitamins in suspected acute myocardial infarction)

L55 ANSWER 9 OF 22 HCA COPYRIGHT 1998 ACS

121:277888 Blood antioxidants and indices of lipid peroxidation in subjects with **angina pectoris**. Duthie, Garry G.; Beattie, James A. G.; Chb, Mb; Arthur, John R.; Franklin, Michael; Morrice, Philip C.; James, W. Philip T. (Scottish Agricultural Statistical Service, Rowett Research Institute, Bucksburn/Aberdeen, UK). Nutrition (Syracuse, N. Y.), 10(4), 313-16 (English) 1994. CODEN: NUTRER. ISSN: 0899-9007.

AB We tested the antioxidant hypothesis of coronary heart disease (CHD) by comparing blood antioxidants, indexes of lipid peroxidn. and classic (CHD) risk factors of 25 subjects with stable **angina pectoris** with 200 matched controls. **Angina** subjects had significantly increased plasma concns. of total cholesterol, low d.

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d 153 1-2 cbib abs hitstr hitind

L53 ANSWER 1 OF 2 HCA COPYRIGHT 1998 ACS

126:338275 Nisoldipine coat-core: a review of its pharmacodynamic and pharmacokinetic properties and clinical efficacy in the management of ischemic heart disease. Langtry, Heather D.; Spencer, Caroline M. (Adis International Limited, Auckland, N. Z.). Drugs, 53(5), 867-884 (English) 1997. CODEN: DRUGAY. ISSN: 0012-6667. Publisher: Adis.

A review with 48 refs. Nisoldipine coat-core is an extended-release once-daily formulation of a dihydropyridine calcium antagonist effective in the treatment of chronic stable **angina** pectoris. With immediate-release formulations of nisoldipine, plasma drug concns. that produce therapeutic effects result rapidly, but are not sustained and do not maintain the effects throughout a 12-h dosage interval. In contrast, with nisoldipine coat-core, a gradual increase in plasma nisoldipine concns. occurs over 12 h and therapeutic concns. are then maintained for the duration of a 24-h dosage interval. In dosages of 10 to 60mg once daily, nisoldipine coat-core controls symptoms of **angina** and improves exercise-induced signs of ischemia in patients with stable **angina**. Compared with placebo, daily nisoldipine coat-core doses of .gtoreq.20mg provide statistically significant increases in total exercise time and time to produce **angina** and a trend towards an increase in the time to produce 1mm ST segment depression, in exercise tests conducted .apprxeq.23 h postdose. When administered in 20 and 40mg daily doses, nisoldipine coat-core produces improvements in exercise test parameters that are similar to those seen with amlodipine 5 or 10 mg/day or regular-release or sustained-release (SR) diltiazem 240 mg/day. The frequency of daily **angina** attacks and consumption of short-acting nitrates are also reduced by nisoldipine to a similar extent to that obsd. with these other agents. After longer term (1 yr) administration of 10 to 60mg daily, improvements in exercise test parameters are maintained, with equiv. anti-ischemic efficacy seen in patients

receiving nisoldipine coat-core alone or with background nitrate or .beta.-blocker therapy. Adverse events assocd. with nisoldipine coat-core are typical of the dihydropyridine class of calcium antagonists, with peripheral edema and headache being most common. Nisoldipine coat-core appears to be assocd. with fewer deaths than placebo, notably in the DEFIANT-II (Doppler Flow and Echocardiog. in Functional Cardiac Insufficiency: Assessment of Nisoldipine Therapy II) study, where only 1 death occurred with nisoldipine compared with 7 in the placebo group. Nisoldipine should not be taken during phenytoin therapy. In addn., **grapefruit juice** should be avoided during nisoldipine therapy and nisoldipine should not be taken concurrently with high-fat meals. Thus, the coat-core formulation of nisoldipine appears to have overcome the limitations of the shorter duration of action of immediate-release nisoldipine. Nisoldipine coat-core is well tolerated and once-daily administration produces a long duration of effective anti-ischemic relief in patients with chronic stable **angina pectoris**.

CC 1-0 (Pharmacology)

L5333 ANSWER 2 OF 2 HCA COPYRIGHT 1998 ACS

74:115882 Citric acid pharmaceutical compositions. Renie, Jeanne Fr. M. FR 6334 681104, 4 pp. (French). CODEN: FMXXAJ. APPLICATION: FR 661213.

AB The use of citric acid (I) as a purgative, as a fluidizing agent for blood, or as a urine pH adjuster may give rise to toxic effects at the doses normally required. By using a combination of I with its alkali metal salts such side-effects are avoided. A formulation presented in a sachet contained 1.3 g I, 2 g mono-Na citrate, 2 g mono-K citrate, 1 mg tartrazine yellow, 40 mg **lemon essence**, 40 mg **orange essence**, 9 mg mandarin essence, and sucrose to 16 g. The compn. was useful in treatment of pain caused by **angina** and rheumatism.

IC A61K

CC 63 (Pharmaceuticals)

ST citrate compns **angina**; rheumatism citrate compns

=> d 155 1-22 ti

L55 ANSWER 1 OF 22 HCA COPYRIGHT 1998 ACS

TI Compositions and methods for inhibiting thrombogenesis

L55 ANSWER 2 OF 22 HCA COPYRIGHT 1998 ACS

TI Use of hydroxyguanidines for treatment or prevention of an ischemic disease

L55 ANSWER 3 OF 22 HCA COPYRIGHT 1998 ACS

TI Compositions and methods for inhibiting thrombogenesis

L55 ANSWER 4 OF 22 HCA COPYRIGHT 1998 ACS

TI Responses to acute myocardial stress and prior drug therapy on plasma levels of antioxidants and oxidants and the proposed role of

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DISEASE; HEART DISEASE; CLASS

50-81-7 (ASCORBIC ACID)

50-99-7 (GLUCOSE)

59-02-9 (ALPHA-TOCOPHEROL)

7235-40-7 (BETA-CAROTENE)

CC General Biology-Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals 00520
Biochemical Studies-Vitamins 10063

Biochemical Studies-Lipids 10066

Nutrition-Fat-Soluble Vitamins *13208

Cardiovascular System-Heart Pathology *14506

Cardiovascular System-Blood Vessel Pathology *14508

Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies
*15002

BC Hominidae 86215

L32 ANSWER 9 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS

AN 91:142181 BIOSIS

DND BA91:78721

TRB RISK OF ANGINA PECTORIS AND PLASMA CONCENTRATIONS OF
VITAMIN A VITAMIN C AND VITAMIN
E AND CAROTENE.

AU RIEMERSMA R A; WOOD D A; MACINTYRE C C A; ELTON R A; GEY K F; OLIVER
M F

CS CARDIOVASCULAR RES. UNIT, UNIVERSITY EDINBURGH, GEORGE SQUARE,
EDINBURGH EH8 9XF, ENGL.

SO LANCET (N AM ED) 337 (8732). 1991. 1-5. CODEN: LANAAI

LA English

AB The relation between risk of angina pectoris and plasma
concentrations of vitamins A, C, and E and
carotene was examined in a population case-control study of 110 cases
of angina, identified by the Chest Pain
Questionnaire, and 394 controls selected from a sample of 6000 men
aged 35-54. Plasma concentrations of vitamins C
and E and carotene were significantly inversely related to the risk
of angina. There was no significant relation with vitamin
A. Smoking was a confounding factor. The inverse relation between
angina and low plasma carotene disappeared and that with
plasma vitamin C was substantially reduced after
adjustment for smoking. Vitamin E remained independently and
inversely related to the risk of angina after adjustment
for age, smoking habit, blood pressure, lipids, and relative weight.
The adjusted odds ratio for angina between the lowest and
highest quantiles of vitamin E concentrations was 2.68 (95%
confidence interval 1.07-6.70; p = 0.02). These findings suggest that
some populations with a high incidence of coronary heart disease may
benefit from eating diets rich in natural antioxidants, particularly
vitamin E.

ST HUMAN LIPID AGE SMOKING CORONARY HEART DISEASE NATURAL
ANTIOXIDANT-RICH DIET EPIDEMIOLOGY

RN 50-81-7 (VITAMIN C)

1406-18-4 (VITAMIN E)
 68-26-8Q, 11103-57-4Q (VITAMIN A)
 Behavioral Biology-Human Behavior *07004
 Biochemical Studies-Vitamins 10063
 Biochemical Studies-Lipids 10066
 Nutrition-Fat-Soluble Vitamins *13208
 Nutrition-Water-Soluble Vitamins *13210
 Nutrition-General Dietary Studies 13214
 Nutrition-Prophylactic and Therapeutic Diets *13218
 Nutrition-Lipids 13222
 Cardiovascular System-General; Methods 14501
 Cardiovascular System-Heart Pathology *14506
 Cardiovascular System-Blood Vessel Pathology *14508
 Psychiatry-Addiction-Alcohol, Drugs, Smoking, etc. *21004
 Toxicology-General; Methods and Experimental *22501
 Gerontology *24500
 Public Health: Epidemiology-Organic Diseases and Neoplasms *37054
 BC Hominidae 86215

L32 ANSWER 11 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS

AN 90:250224 BIOSIS

DN BR38:116812

TI LOW PLASMA VITAMINS E AND C INCREASED RISK OF
ANGINA IN SCOTTISH MEN.

AU RIEMERSMA R A; WOOD D A; MACINTYRE C C A; ELTON R; GEY K F; OLIVER M

CS CARDIOVASC. RES. UNIT, UNIV. EDINBURGH, EDINBURGH EH8 9XF, SCOTL.
 SO DIPLOCK, A. T., ET AL. (ED.). ANNALS OF THE NEW YORK ACADEMY OF
 SCIENCES, VOL. 570. VITAMIN E: BIOCHEMISTRY AND HEALTH IMPLICATIONS;
 CONFERENCE, NEW YORK, NEW YORK, USA, OCTOBER 31-NOVEMBER 2, 1988.
 XIII+555P. NEW YORK ACADEMY OF SCIENCES: NEW YORK, NEW YORK, USA.
 ILLUS. 0 (0). 1989 (1990). 291-295. CODEN: ANYAA9 ISBN:
 0-89766-536-8(PAPER); 0-89766-535-X(CLOTH) ISSN: 0077-8923

DT Conference

LA English

ST HUMAN RISK ASSESSMENT SERUM CHOLESTEROL BLOOD PRESSURE SMOKING LOW
FATTY ACID LEVELS PLASMA PHOSPHOLIPIDS ANTIOXIDANT

RN 57-88-5 (CHOLESTEROL)

CC General Biology-Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals 00520

Behavioral Biology-Human Behavior 07004

Biochemical Studies-General 10060

Biochemical Studies-Lipids 10066

Biochemical Studies-Sterols and Steroids 10067

Metabolism-Energy and Respiratory Metabolism *13003

Metabolism-Lipids *13006

Metabolism-Sterols and Steroids *13008

Metabolism-Fat-Soluble Vitamins *13016

Metabolism-Water-Soluble Vitamins *13018

Nutrition-Malnutrition; Obesity *13203

Nutrition-Fat-Soluble Vitamins *13208

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Medicinal compsn. for the treatment of **stenocardia** attacks
contains (in wt.%): nonachazin(I) 1.59-14.57; 96% ethanol 4.04-32.3;
ascorbic acid 0.2-0.21; sodium metabisulphite
0.09-0.1; sodium chloride 0.24-0.26 and distilled water 65.54-80.86.
The compsn. is quick-acting and reduces the severity and the
duration of cardiac attack.

=> file biosis

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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNS) PRESENT
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L27 ANSWER 1 OF 1 BIOSIS COPYRIGHT 1998 BIOSIS

AN 80:130874 BIOSIS

DN BA69:5870

TI CONTINGENCY MANAGEMENT OF ADHERENCE TO A COMPLEX MEDICAL REGIMEN IN
AN ELDERLY HEART PATIENT.

AU DAPCICH-MIURA E; HOVELL M F

CS LAB. STUD. BEHAV. MED., STANFORD UNIV. SCH. MED., SUITE 234, 730
WELCH RD., PALO ALTO, CALIF. 94304, USA.

SO BEHAV THER 10 (2). 1979. 193-201. CODEN: BHVTAK ISSN: 0005-7894

LA English

AB Whether token reinforcement could improve an elderly heart patient's
adherence to his complex medical regimen was investigated. Using a
multiple-baseline and reversal single-case experimental design, it
was demonstrated that the reinforcement contingency was responsible
for increasing his walking to more than twice/day, consumption of
orange juice to an average of almost 3 glasses/day
and consumption of 3 separate pills 3 times/day. A cessation of
angina and an improvement in family relationships also
occurred.

ST **ANGINA** FAMILY RELATIONSHIP TOKEN ECONOMY

CC Social Biology; Human Ecology 05500

Behavioral Biology-Human Behavior *07004

Behavioral Biology-Conditioning 07005

Physiology, General and Miscellaneous-Exercise and Physical Therapy
12010

Movement 12100

Pathology, General and Miscellaneous-Therapy 12512

Nutrition-General Studies, Nutritional Status and Methods 13202

Food Technology-Fruits, Nuts and Vegetables 13504

Cardiovascular System-Heart Pathology *14506

Please amend claim 1 as follows:

1. (amended) A method of preventing the reoccurrence of chest pain associated with the heart, which method comprises:

- 62
- (a) noticing a pain in the chest; and then shortly thereafter
 - (b) taking an effective amount of lime juice into the body to alleviate the chest pain.


112 What is effective?

REMARKS

Claims 14-17 have been added to the application, and claim 1 has been amended to clarify the invention.

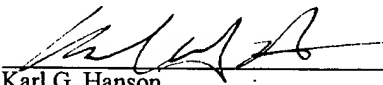
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Respectfully submitted,


Karl G. Hanson
Attorney for Applicant
Registration No. 32,900

3M Office of Intellectual Property Counsel
P.O. Box 33427
St. Paul, Minnesota 55133-3427
Telephone: (612) 736-7776
Facsimile: (612) 736-3833

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Karl G. Hanson

Dated: 1/12/98

What is claimed is:

5 1. A method of preventing the reoccurrence of chest pain associated with the heart, which method comprises:

- (a) noticing a pain in the chest; and then shortly thereafter
- (b) taking lime juice into the body to alleviate the chest pain.

2. The method of claim 1, wherein the chest pain is angina pectoris.

10 3. The method of claim 1, wherein the lime juice enters the body by consuming it orally.

15 4. The method of claim 2, wherein the lime juice is consumed in concentrated form by taking at least one half teaspoon of frozen concentrated lime juice or limeade.

20 5. The method of claim 1, further comprising:
preventing the reoccurrence of chest pain by taking lime juice into the body daily.

6. The method of claim 5, wherein at least one cup of lime juice is consumed orally daily.

25 7. The method of claim 6, wherein 2 to 5 cups are consumed daily.

8. The method of claim 6, wherein 2 to 3 cups are consumed daily.

9. A method of treating angina pectoris, which method comprises:

- (a) noticing the onset of an angina attack; and then shortly thereafter
- (b) taking an effective amount of lime juice into the body.

